

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : **10/780,484**  
Applicants : **David B. Rozema et al.**  
Filed : **02/17/2004**  
Art Unit : **1633**  
Examiner : **Epps Ford, Janet L.**  
Docket No. : **Mirus.030.16.4**

Commissioner of Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R. §1.132**

Dear Commissioner:

I, Dr. David B. Rozema, hereby declare as follows:

1. I have a Doctorate in Chemistry from the University of Wisconsin, Madison.
2. I am familiar with the above captioned application and US 2002/0107330, and a co-inventor of US 20010036926 and 7,087,770 .
3. An S-nitrosothiol group is a sulfur-containing nitrite having the general formula: R-S-N=O. These compounds are often thermally unstable with respect to formation of the disulfide and nitric oxide:  $2 \text{RSNO} \rightarrow \text{RSSR} + 2 \text{NO}$ . S-Nitrosothiols also release  $\text{NO}^+$  upon treatment with acids:  $\text{RSNO} + \text{H}^+ \rightarrow \text{RSH} + \text{NO}^+$ . S-Nitrosothiols can also transfer nitroso groups to other thiols:  $\text{RSNO} + \text{R}'\text{SH} \rightarrow \text{RSH} + \text{R}'\text{SNO}$ .

The cleavage of the S-nitroso group to a thiol and nitric oxide does not in any way involve an amine group. As defined by the International Union of Pure and Applied Chemistry amines are compounds formally derived from ammonia by replacing one, two or three hydrogen atoms by hydrocarbyl groups (a hydrocarbyl group is formed by removing a hydrogen atom from a hydrocarbon). Neither the starting nitroso group nor either of the products have an amine functional group. The S-nitroso group may be attached to a molecule that contains an amine, but the S-nitroso group does not in any way involve the modification or production of an amine group.

4. The teachings in Wolff et al. (US 20010036926 and 7,087,770) also do not disclose the reversible modification of amines. US 20010036926 and 7,087,770 teach the use of disulfide bonds to reversibly link two molecules. US 20010036926 and 7,087,770 teach an amine function group may be modified to form an amide. However, subsequent cleavage of the modifier does not reform an amine. US 20010036926 and 7,087,770 do not teach the labile modification of an amine such that cleavage of the modifier restores the amine.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



16/27/08  
date

Dr. David B. Rozema